

REMARKS

FORMAL MATTERS:

Claims 15, 16 and 18-23 are now pending in this application.

Claims 15 and 23 have been amended to more particularly point out and distinctly claim the invention. The amendments to claims 15 and 23 are fully supported within previously pending now canceled claim 17 and within the specification such as within the examples and within the myeloma cell lines described in the specification at page 9, line 36 – page 10, line 5. Claim 18 is formally amended in view of the cancellation of claim 17. No new matter has been added.

In that applicants have incorporated limitations contained within previously pending now canceled claims into the independent claims these amendments are believed to be permissible under 37 C.F.R. §1.116 and entry of the amendments is respectfully requested.

Rejection under 35 U.S.C. §112

Claims 15-23 were rejected under 35 U.S.C. §112, first paragraph. In support of the rejection it was argued that the specification was not enabling with respect to methods which utilize all types of immortal cell lines. However, the rejection indicated that the specification was enabling with respect to the use of myeloma cell lines. Applicants do not acquiesce to the rejection. However, applicants wish to expedite prosecution. Accordingly, the independent claims 15 and 23 have been amended to indicate that the immortal cell line is a recombinant myeloma cell line. Accordingly, the rejection is believed to have been rendered moot.

Rejection under 35 U.S.C. §103

Claims 15-23 were rejected under 35 U.S.C. §103 as unpatentable over published application and issued Patent to Wood et al. in view of Mendez et al. The rejection is traversed as applied and as it might applied to the presently pending claims.

In accordance with Wood et al. the production of the hybridoma is in accordance with Kohler and Milstein. Thus, the hybridoma is made using the conventional methodology of fusing the spleen cells with a myeloma cell line. There is no disclosure of fusing B-cells of a transgenic mouse with another cell line. Further, there is no disclosure of fusing the B-cells with a recombinant myeloma cells line as claimed by applicants. The rejection argues that it would be obvious to combine the teachings of

Mendez et al. with Wood et al. This would need to be done in order to produce hybridoma by fusing a B-cell of a transgenic mouse with a recombinant myeloma cell line. Further, Wood et al. is needed to show transfecting hybridoma cells to improve antibody production.

The rejection appears to recognize that Wood et al. do not disclose introducing the exogenous nucleotide sequences into hybridoma cell lines of the type produced in accordance with applicants' method. However, the rejection argues that in view of Mendez et al. such a combination would be obvious. This rejection is, to an extent, logically inconsistent with the 35 U.S.C. §112, first paragraph rejection. That rejection argues that due to the unpredictability of this science one skilled in the art could not determine if the invention would work with other types of immortal cell lines and is specifically restricted to situations where the hybridoma is produced using a myeloma cell line. Applicants recognize different legal standards with respect to enablement under 35 U.S.C. §112 and obviousness under 35 U.S.C. §103. However, it is recognized that there is a degree of unpredictability with respect to this art. Here, applicants have clearly shown fusing a B cell of a transgenic mouse with a myeloma cell line and then transfecting that cell line in a particular manner in order to substantially enhance antibody production. This substantially enhanced antibody production is clearly demonstrated by applicants within Table 2 and also shown within the same table of the corresponding PCT application WO 00/58499 in Table 2 on page 26. The ability to obtain such improved results utilizing a different type of hybridoma other than that taught by Wood et al. is not entirely predictable. Notwithstanding this position Wood et al. is distinguishable from the present invention due to the type of genetic material used to transfect the hybridoma as described further below.

The expression vectors utilized by Wood et al. to transfect the hybridoma are comprised of multiple different sequences. However, in accordance with applicants' invention applicants transfect the cell with "an exogenous nucleotide sequence which encodes a heavy chain polypeptide identical to the heavy chain polypeptide express by the endogenous immunoglobulin heavy chain". To obtain the transformant of applicants invention it would be necessary for Wood et al. to eliminate certain sequences and to specifically produce the transformant in accordance with Applicants invention. Wood et al. do not teach towards significantly increasing monoclonal antibodies from a recombinant hybridoma by introducing an exogenous nucleotide sequence which encodes a heavy chain polypeptide identical to the heavy chain polypeptide expressed by the endogenous immunoglobulin heavy chain. Absent this teaching it is applicants position that it is not *prima facie* obvious to combine Wood et al. and Mendez et al. to obtain applicants invention.

Notwithstanding the question of whether it is obvious to combine these references applicants have demonstrated improved unexpected results. Specifically, results shown by Applicants within Table 2 clearly demonstrate that applicants have been able to substantially increase the production of antibodies. Specifically, applicants refer to the parental line 15-4 shown in Table 2 on page 25. This line shows and increase to about 95.3 ug/ml as compared to an amount of 37.3 ug/ml.

Based on the data provided by Applicants even if it were *prima facie* obvious to combine Wood et al. with Mendez et al. the specifically claimed invention would not be obtained. Further, even if it were *prima facie* obvious to combine the references in the manner suggested within the rejection applicants have overcome that *prima facie* case of obviousness by demonstrating improved unexpected results. In view of such reconsideration and withdrawal of the rejection is respectfully requested.

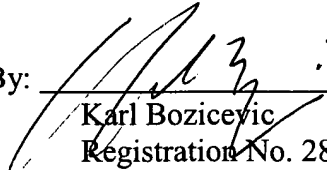
CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SHIM-013.

Respectfully submitted,
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Date: 31/may/05

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